UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/308,080	10/28/1999	FRANK J. GONZALEZ	15280-271100	5674

7590 07/02/2002

KEVIN L BASTIAN
TOWNSEND & TOWNSEND & CREW
TWO EMBARCADERO CENTER
8TH FLOOR
SAN FRANCISCO, CA 94111

EXAMINER
STEADMAN, DAVID J

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 07/02/2002 19

Please find below and/or attached an Office communication concerning this application or proceeding.

19

Office Action Summary	Application No.	Applicant(s)	
	09/308,080	GONZALEZ ET AL.	
	Examiner	Art Unit	
	David J. Steadman	1652	

-- The MAILING DATE of this communication appears on the cover sh et with the corresp ndence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 April 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11,15-17 and 20-28* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11,15-17 and 20-28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Pri rity under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *18* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Status of the Application

Claims 1-11, 15-17, and 20-28 are pending in the application.

Applicants' amendment to claims 1-11, 15-17, and 20-28 in Paper No. 17, filed 04/15/02 is acknowledged.

Applicants' arguments presented in Paper No. 17 have been fully considered and are deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

The text of those sections of Title 35 U.S. Code not included in the instant action can be found in a prior Office action.

Claim Rejections - 35 USC § 112, Second Paragraph

1. Claims 1-5, 8, 10, 11, 15, 20 22, 24, and 26 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

2. Claim 1 (claims 2-5 dependent therefrom) is confusing in the recitation of "wherein said gene the substitution of the G residue with an A residue at said position". As written, it is unclear as to the meaning the term. It is suggested that applicants clarify the meaning of the term. In order to further prosecution, the examiner has interpreted the term as "wherein the substitution of the G residue with an A residue at said position".

3. Claims 3, 8, 10, 11, 15, 20, 22, 24, and 26 are rejected as being unclear in the recitation of the term "subregion... ...of SEQ ID NO:1" in claims 3, 8, 10, 15, and 26 and "subregion... ...located within 100 nucleotides of the position indicated as nucleotide 434 of SEQ ID NO:1" in claims 11, 20, 22, and 24. The terms are not defined by the claims or the specification and the "subregion" of SEQ ID NO:1 or "subregion" located within 100 nucleotides of nucleotide 434 of SEQ ID NO:1 is unclear. It is suggested

that applicants identify the specific nucleotides of SEQ ID NO:1 that are encompassed within the scope of the terms.

Claim Rejections - 35 USC § 112, First Paragraph

4. The written description rejection of claims 1-4, 8-10, 15-17, 20, 22, 24, 26, and 27 under 35 U.S.C. 112, first paragraph, is maintained. The rejection was fully explained in a previous Office action.

It is noted that applicants' arguments are confusing as they appear to respond to the instant rejection with arguments mostly relating to a scope of enablement rejection and *not* the instant written description rejection. While the arguments appear to respond an enablement-type rejection, the examiner has attempted to respond to applicants' arguments in order to further prosecution of the application.

Regarding the written description of the DPD genomic DNA, applicants argue (pages 11 and 12 of Paper No. 17) claim 1 recites the functional limitation of causing a splicing defect in an otherwise functional splicing region. Applicants argue the specification teaches how to detect G or A residue. Applicants argue the method of detecting G or A would be applicable to any human DPD genomic DNA as DPD nucleic and amino acid sequences are highly conserved. Applicants argue that inoperable embodiments of an invention do not render a claim nonenabled. Applicants' argument has been fully considered but is not found persuasive to overcome the instant rejection.

Regarding the written description of the primer, applicants argue (pages 12-15 of Paper No. 17) the claims are drawn to primers that are complementary to a subregion of human of SEQ ID NO:1 or a subregion within 100 nucleotides of position 434 of SEQ ID NO:1. Applicants argue the teaching of a single species of the genus of recited primers provides a multitude of subregions to generate other primers. Applicants argue that in a highly conserved gene, variations of sequence within one subregion do not affect the operability of primers directed to other subregions of the variant gene. Applicants argue three primers is sufficient to describe the genus of recited primers. Applicants' argument has been fully considered but is not found persuasive to overcome the instant rejection.

Regarding the written description of the restriction endonuclease, applicants argue (page 13 and 14 of Paper No. 17) that undue experimentation is not required to practice the methods of claims 4 and 9 or to make the kits of claims 17 and 27 as has only to search the existing databases for endonucleases with the required specificity. Upon search of a database, applicants allege to have identified four different endonucleases that cleave the recognition sequence ACGT. Applicants' arguments have been fully considered but are not found persuasive to overcome the instant rejection.

In response to all of applicants' arguments, the specification teaches only a single representative species of human intronic DPD genomic DNAs comprising nucleotide 434 of SEQ ID NO:1, i.e., SEQ ID NO:1, three representative species of PCR primers as encompassed by the claims, i.e., SEQ ID NOs:2-5 and a single representative species of restriction endonucleases, i.e., MaeII. The specification has provided only a single species of a human genomic DPD sequence, i.e., SEQ ID NO:1, which is insufficient to describe the entire genus of human genomic DPD sequences. Therefore, because the structural information needed to generate the claimed primers and methods of use thereof is derived from the genomic sequence, applicants have not sufficiently described the genus of human genomic DPD sequences such that one of skill in the art could visualize the entire genus of recited primers. Furthermore, at the time of the invention, the prior art did not disclose the relative homogeneity of DPD genomic DNA sequences. Given this lack of description of representative species encompassed by the genus of the claim, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention.

5. The scope of enablement rejection of claims 4, 9, 17, and 27 are rejected under 35 U.S.C. 112, first paragraph, is maintained. The rejection was fully explained in a previous Office action.

Applicants argue (page 13 and 14 of Paper No. 17) that undue experimentation is not required to practice the methods of claims 4 and 9 or to make the kits of claims 17 and 27 as has only to search the existing databases for endonucleases with the required specificity. Upon search of a database, applicants allege to have identified four different endonucleases that cleave the recognition sequence ACGT.

Applicants' arguments have been fully considered but are not found persuasive to overcome the instant rejection.

It is noted that the examiner has attempted without success to locate the printout of the database search allegedly performed by applicants in identifying restriction endonucleases that recognize ACGT (see page 13, bottom of Paper No. 17). It is also noted that claims 4, 9, 17, and 27 are not so limited to a restriction endonuclease that cleaves at ACGT, but are so broad as to encompass a method of detecting a G or A nucleotide at position 434 of SEQ ID NO:1 *any* restriction endonuclease or a kit comprising *any* restriction endonuclease that cleaves a human DPD having a G nucleotide at position 434 of SEQ ID NO:1. The specification provides guidance only for use of MaeII for detection of G at position 434 of SEQ ID NO:1. The specification does not provide guidance for using *any* restriction endonuclease. While many restriction endonucleases that recognize a core sequence of ACGT may be identified by database searching, it is not clear as to whether these restriction enzymes are further limited in sequence specificity by recognizing additional flanking nucleotides of the sequence ACGT. The specification has provided only a single example of a restriction endonuclease that recognizes ACGT, i.e., MaeII. Thus, the quanity of experimentation required to identify the broad scope of enzymes encompassed by the methods of claims 4 and 9 or the kits of claims 17 and 27 would constitute undue experimentation.

Claim Rejections - 35 USC § 103

6. The rejection of claims 10, 11, 15, and 24 under 35 U.S.C. 103(a) as being unpatentable over Gonzalez et al. in view of Meinsma et al. is maintained. The rejection was fully explained in a previous Office action.

Applicants argue the specific sequence of the intronic DNA cannot be obvious. Applicants argue the existence of a method for gene cloning and sequencing and the motivation to sequence a specific gene is not sufficient to render obvious a particular DNA molecule. Applicants' arguments have been fully considered but are not found persuasive to overcome the instant rejection.

It is noted that the prior art provides more than a mere motivation to generate the recited primers of the rejected claims. Based on the teachings of Gonzalez et al. and Meinsma et al., one of ordinary skill in the art would have known the location of the mutation in the genomic DNA and would have sufficient motivation to create primers to screen for said mutation. Furthermore, one of ordinary skill in the art at the time of the invention would have been able to use primers designed based on the human DPD cDNA sequence, which was known in the art at the time of the invention as acknowledged by Meinsma et al. (page 2, right column), to sequence between exons using human genomic DNA in order to determine the intronic sequences of human DPD genomic DNA. By comparing the sequences of human DPD genomic and complementary DNA, one of ordinary skill in the art would have identified the intron/exon boundary as described by Gonzalez et al. and Meinsma et al. and would have been motivated to generate the primers as claimed in claims 10, 11, 15, and 24 because of Gonzalez et al. who teach that the intron-exon boundaries of the DPD gene are being determined in order to develop a convenient screening assay for the analysis of cancer patients having DPD gene mutations, and that by determining the intron-exon boundaries of the DPD gene, specific PCR primers could be designed to analyze for mutant DPD genes using a PCR-based screening procedure.

Conclusion

7. No claim is in condition for allowance. All claims are rejected.

Applicant's amendment to claims 1-5, 8, 10, 11, 15, 20 22, 24, and 26 necessitated the new ground(s) of rejection presented in this office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Steadman, whose telephone number is (703) 308-3934. The examiner can normally

be reached Monday-Friday from 8:00 am to 4:30 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, can be reached at (703) 308-3804. The FAX number for this Art Unit is (703) 308-4242. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Art Unit receptionist whose telephone number is (703) 308-0196.

David J. Steadman, Ph.D.

NASHAAT T. NASHED PHD.
PRIMARY EXAMINER